Methods: Recipient C57Bl/6 mice received 13 Gy of total body irradiation and were rescued with BM obtained from femurs of donor C57Bl/6 mice. Resident AMs and recruited lung PMNs were harvested 3 to 5 weeks post-BMT and their eicosanoid profile were examined. We measured the Fc and non-Fc mediated phagocytosis and killing of AMs and PMNs post-BMT. Indomethacin, a PG inhibitor, was used to block PGE2 production in vitro and in vivo.
Results: BMT AMs produce 125-times more PGE2 than control AMs and BMT PMNs produce 27-fold more PGE2 than control PMNs. We have shown that the increased susceptibility of BMT mice correlates with defective AM phagocytosis and killing of Gram-negative bacteria. Interestingly, PMNs from BMT mice do not display defective phagocytosis, but do show a defect in their ability to kill ingested Gram-negative bacteria. The pharmacologic blockade of prostaglandin production by indomethacin in vitro restores AM phagocytosis and killing and PMN killing. In addition, treatment with indomethacin restores host defense to *P. aeruginosa* in vivo.
Conclusions: We show that eicosanoid dysregulation post-BMT inhibits the effectiveness of the innate immune response. Inhibiting PGs in vitro and in vivo restores impaired pulmonary host defense post-BMT.

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Increased Susceptibility to *Gammaherpesvirus* Post-Bone Marrow Transplantation

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Background: Bone marrow transplantation (BMT) is used in the treatment of various malignancies. The success of BMT is limited by multiple complications including pulmonary infections both pre-engraftment and after engraftment has occurred. We previously demonstrated that mice after BMT have an increased susceptibility to Gram-negative bacterial pneumonia after engraftment. This appears to be due to impaired lung innate immunity with defective phagocytosis in alveolar macrophages, and defective killing in lung neutrophils. Response to vaccination is diminished in patients post-BMT indicating that there are adaptive immune defects as well. To further elucidate the adaptive immune defects in lungs post-BMT, we analyzed a lung infection with murine gammaherpesvirus-68 (MHV-68). MHV-68 is a ds-DNA virus that is most similar to *Epstein Barr virus* (EBV) and *Kaposi sarcoma-associated herpesvirus* (KSHV) in humans.
Objective: Our hypothesis is that dysregulation in the adaptive immune response in the lungs post-BMT leads to increased susceptibility to viral infection.
Methods: Syngeneic BMT was performed in recipient C57Bl/6 mice receiving 13 Gy of total body irradiation, rescued with bone marrow obtained from the femurs of donor C57Bl/6 mice. Control (untransplanted) and BMT mice were infected with 5×10^4 plaque forming units (PFUs) MHV-68 intranasally at 6 weeks post-BMT. PFUs were measured from lung homogenates at days 3, 5, 7, 9, and 14 post-infection. Cell counts and differentials were performed and lymphocyte subsets were analyzed with flow cytometry. Cytokine levels were measured using ELISA.
Results: Mice that have undergone BMT have 25-times the PFUs at day 7 post-infection versus control mice. There is an increase in the percentage of neutrophils, and a decrease in lymphocytes in BMT mice versus control mice. There is a decrease in the percentage of CD8+ T-cells, but no change in CD4+ T-cells, B-cells, or NK cells. There is no difference in TNF alpha levels in BMT versus control mice post infection. While IFN-gamma increased in control mice, no increase was seen in BMT mice post infection.
Conclusion: Mice post-BMT have an increased susceptibility to lytic lung infection with MHV-68 after full engraftment has occurred. This finding is likely related to both innate and adaptive immune defects.

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Human CMV gB Genotype 1 is Dominant in Hematopoietic Stem Cell Transplant Recipients in Korea: The Association of gB Genotype with CMV Diseases?

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Background & Objectives: The *cytomegalovirus* (CMV) glycoprotein B (gB) is the major envelope glycoprotein, encoded by the UL55 gene. Based on sequence variation in the UL55 gene, CMV can be classified into four gB genotypes. Previous studies have suggested there could be an association between CMV gB genotype and clinical outcome in the immunocompromised hosts. The goal of this study was to determine the distribution of CMV gB genotypes and the effect of gB genotype in the development of CMV diseases in hematopoietic stem cell transplant (HSCT) recipients in Korea.